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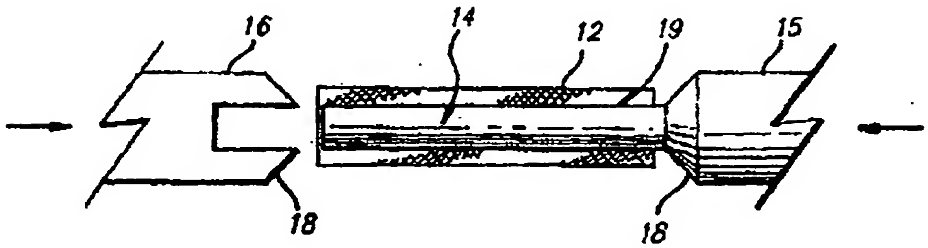
(54) Polymer-coated stent structure

(57) The thickness of a polymer coating applied to the interior surface of a stent (12) precisely is controlled by fitting a mandrel (14 and 15, 26) within its interior. Fitment of an exterior mold (20) serves to additionally control the thickness of polymer on the exterior surface of the stent. Alternatively, a pre-formed sheath of polymer is fitted to the interior of the stent, whereby the subsequent application of polymer not only causes the exterior to become coated but also causes the sheath to become adhered to the stent.

FIG. 1



Description

BACKGROUND OF THE INVENTION

[0001] This invention relates generally to expandable intraluminal vascular grafts, commonly referred to as stents, and more particularly concerns the coating of metal stents with polymer materials capable of carrying and releasing therapeutic drugs.

[0002] Stents are implanted within vessels in an effort to maintain the patency thereof by preventing collapse and/or by impeding restenosis. Implantation of a stent typically is accomplished by mounting the stent on the expandable portion of a balloon catheter, maneuvering the catheter through the vasculature so as to position the stent at the desired location within the body lumen, and inflating the balloon to expand the stent so as to engage the lumen wall. The stent automatically locks into its expanded configuration allowing the balloon to be deflated and the catheter to be removed to complete the implantation procedure.

[0003] It often is desirable to provide localized pharmacological treatment of a vessel at the site being supported by the stent and it has been found convenient to utilize the stent as a delivery vehicle for such purpose. However, because of the mechanical strength that is required to properly support vessel walls, stents typically must be constructed of metallic materials which are not capable of carrying and releasing drugs. Various polymers, on the other hand, are quite capable of carrying and releasing drugs but generally do not have the requisite mechanical strength. A previously devised solution to such dilemma has been the coating of the metallic structure of a stent with a polymer material, in order to provide a stent that is capable of both supporting adequate mechanical loads and of delivering drugs.

[0004] Various approaches previously have been used to join polymers to metallic stents, including dipping, spraying and conforming processes. However, such methods have failed to provide an economically viable method of applying a very even coating of polymer on the stent surfaces or the ability to economically apply different thicknesses or different polymers in different areas on the same stent.

[0005] The prior art has been unable to overcome these shortcomings and a new approach is needed for effectively and economically applying a polymeric material to a metallic stent with a high degree of precision.

SUMMARY OF THE INVENTION

[0006] Certain embodiments of the invention seek to provide a method of joining a polymeric material with a metallic stent that overcomes the disadvantages and shortcomings of previously employed processes. According to preferred embodiments, very precisely controlled thicknesses of polymer can be applied to selected surfaces of a stent. The resulting stent has the mechanical strength necessary to properly support a blood vessel while being capable of delivering a pre-selected quantity of drug or drugs over a desired period of time. Moreover, the attached polymer does not interfere in the deployment of the stent and therefore allows the stent to be freely expanded.

[0007] These preferred methods call for the use of mandrels and/or molds to apply precise amounts of polymer to the stent surfaces. Moreover, advantageous positioning of such implements relative to the stent allow the thickness of the polymer to be varied from surface to surface. It thereby readily is possible to apply a thicker layer of polymer to the blood-facing side of the stent than to the vessel-facing side or vice versa. Additionally, by employing successive molding operations, different polymers, selected for their differentiated ability to absorb and release different therapeutic agents, can be applied to selected surfaces of the stent. Alternatively, the polymer may be applied to one side of the stent as a preformed sheath, while the subsequent molding operation not only serves to coat the opposite surface of the stent but also serves to adhere the pre-formed sheath to the stent. Upon implantation of a stent with such differentiated surfaces, it thereby is possible to directly expose the vessel wall to one therapeutic agent while exposing the blood to a different therapeutic agent. Alternatively, it is possible to load polymers with different carrying capacities of a particular therapeutic agent to thereby deliver different concentrations in a desired pattern.

[0008] The method of the present invention includes a number of alternative embodiments, including the use of various combinations of mandrel configurations, and exterior molds. The polymer is applied by either a dip coating, pull trusion or injection molding process. The embodiments of the method of the present invention insure that very precisely dimensioned coatings result even after the drying and the cooling processes are completed. A final serration or separation step may be necessary for some stent configurations in order to restore the desired flexibility and expandability to the stent. A laser is used for such purpose, to quickly and precisely cut and/or remove polymer from various locations on the coated stent.

[0009] These and other features and advantages of the embodiments of the present invention will become apparent from the following detailed description of a preferred embodiment which, when taken in conjunction with the accompanying drawings, illustrates by way of example the principles of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] FIGURE 1 is a cross-sectional view of a mandrel being positioned within a stent.

[0011] FIG. 2 is a cross-sectional view of a mandrel in position within a stent and an exterior mold positioned thereabout.

[0012] FIG. 3 is a cross-sectional view of a mandrel

being inserted into a pre-formed sheath-containing stent.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0013] The figures generally illustrate the techniques used to apply a polymer to a stent. Any of a variety of stent configurations may be subjected to the coating process described herein, including but not limited to multi-link or slotted tube-type designs. The metals from which such stents are formed may include stainless steels, nickel titanium (NiTi), and tantalum, among others. The polymer or the combination of polymers that are applied to the stent are selected for the ability to carry and release, at a controlled rate, various therapeutic agents such as anti-thrombogenic or anti-proliferative drugs. The polymeric material of the method preferably comprises a biodegradable, bioabsorbable polymeric film that is capable of being loaded with and of releasing therapeutic drugs. The polymeric materials preferably include, but are not limited to, polycaprolactone (PCL), poly-DL-lactic acid (DL-PLA) and poly-L-lactic acid (L-PLA) or lactide. Other biodegradable, bioabsorbable polymers such as polyorthoesters, polyiminocarbonates, aliphatic polycarbonates, and polyphosphazenes also may be suitable, and other non-degradable polymers capable of carrying and delivering therapeutic drugs also may be suitable. Examples of non-degradable synthetic polymers are those sold under the trademarks PARYLENE and PARYLAST by Advanced Surface Technology, Co. of Billerica, Massachusetts, U.S.A. and polyurethane, polyethylene, polyethylene teraphthalate, ethylene vinyl acetate, silicone and polyethylene oxide (PEO).

[0014] Examples of therapeutic drugs, or agents that can be combined with the polymeric materials, include antiplatelets, anticoagulants, antifibrins, antithrombins and antiproliferatives. Examples of antiplatelets, anticoagulants, antifibrins and antithrombins include, but are not limited to, sodium heparin, low molecular weight heparin, hirudin, argatroban, forskolin, vapiprost, prostacyclin and prostacyclin analogues, dextran, D-phe-pro-arg-chloromethylketone (synthetic antithrombin), dipyridamole, glycoprotein IIb/IIIa platelet membrane receptor antibody, recombinant hirudin, thrombin inhibitor (available from the Biogen Corp. of Cambridge, Massachusetts, U.S.A.), and an antiplatelet drug sold under the trademark 7E-3B by the Centocor, Inc. of Malvern, Pennsylvania, U.S.A.) Examples of cytostatic or antiproliferative agents include angiopeptin (a somatostatin analogue available from the Ibsen Company of, angiotensin-converting enzyme inhibitors such as CAPTOPRIL (available from Squibb Pharamaceuticals of Cincinnati, Ohio, U.S.A.), CILAZAPRIL (available from Hoffmann-La Roche, Inc, of Carleton, Michigan, U S.A.), or LISINOPRIL (available from Merck Pharmaceuticals of Kouts, Indianan, U.S.A.); calcium channel blockers (such as NIFEDIPINE), colchicine, fibroblast growth factor (FGF) antagonists, fish oil (omega 3-fatty acid), histamine antagonists, LOVASTATIN (an inhibitor of HMG-CoA reductase, a cholesterol-lowering drug also available from Merck Pharmaceuticals), methotrexate, monoclonal antibodies (such as to PDGF receptors), nitroprusside, phosphodiesterase inhibitors, prostaglandin inhibitor (available from Glaxo Wellcome, Inc. of Durham, North Carolina, U.S.A.), seramin (a PDGF antagonist), serotonin blockers, steroids, thioprotease inhibitors, triazolopyrimidine (a PDGF antagonist), and nitric oxide. Other therapeutic drugs or agents which may be appropriate include alpha-interferon and genetically engineered epithelial cells, for example.

[0015] While the foregoing therapeutic agents have been used to prevent or treat restenosis, each is provided by way of example and collectively the examples are not meant to be limiting, since other therapeutic drugs may be developed which are equally applicable for use with the present invention. The treatment of diseases using the above therapeutic agents is known in the art. Further, the calculation of dosages, dosage rates and appropriate duration of treatment are previously known in the art.

[0016] FIG. 1 illustrates a method embodying the invention it its simplest form. The stent 12 is first slipped onto a mandrel in the form of a core pin 14 after which a pin cap 16 is fitted to its distal end. The core pin extends from a proximal section 15 of increased diameter similar to the outer diameter of the pin cap. As these two pin components are advanced towards one another, the tapered configurations of the corresponding receiving surfaces 18 automatically cause the stent to become centered about the core pin. The interference fit between the core pin and pin cap insures that the components remain assembled and properly aligned during subsequent handling and processing. The pin is precisely dimensioned to provide the desired spacing 19 between the exterior surface of the pin and the interior surface of the stent. Such fixation of the stent also serves to minimize the area of contact between the stent and mandrel, which is limited to only two very narrow circles on the opposite edges of the stent.

[0017] The assembly subsequently is submersed in the selected polymer while the polymer is in a liquid or molten state. Adjustment of the viscosity of the polymer may be necessary in order to insure free access to the space between the core pin and the stent via the link spacings or slots. This adjustment may be achieved either by thermal or chemical means and is best optimized by empirical methods as are well know in the art The presence of the pin strictly limits and thereby precisely controls the maximum thickness of polymer that can be applied to the interior surface of the stent. Moreover, prolonged or repeated contact with the polymer allows a substantially thicker layer of polymer to be built up on the exterior of the stent while the thickness of the interior layer remains constant. Alternatively, subsequent expo-

sure to a second polymer allows the exterior, i.e., vessel side of the stent, to be coated with a different polymer than is attached to the interior surface of the stents, i.e., blood side. After the polymer or polymers have all solidified or have been cured sufficiently, the core pin and pin cap are removed.

[0018] As an alternative to the submersion or dipping technique, the core pin/stent assembly is fitted to the exit port of an extruder and the polymer is applied to the stent using a pull trusion technique well known in the art. Selection of the appropriate viscosity of the polymer again is critical, not only to ensure perfusion of the polymer through openings in the stent and into the space between the stent and the core pin, but also to achieve adequate coverage.

[0019] FIG. 2 illustrates a further altenative embodimemt of the present invention wherein an exterior mold is used in addition to the core pin described above. The stent 12 again first is mounted about the core pin 14 and the pin cap 16, after which the entire assembly is fitted inside an external mold 20. The stent therehy is secured in position so as to define a precise spacing 19 between the exterior of the core pin 16 and the interior surface of the stent and between the exterior surface of the stent and the interior of the external mold 21. Polymer subsequently is injected either via any number of routes, including through a passage extending through the core pin 14 or through the external mold 20. The viscosity of the polymer must be selected to facilitate its flow into the mold and through the stent to insure that an uninterrupted coating of the stent is achieved. Conditions that affect the viscosity requirements include, but are not limited to, the anticipated temperatures, cooling rates, molding time, orifice sizes, molding pressure, and the particular metal from which the stent is formed, etc. The appropriate viscosity easily is selected by one skilled in the art using simple empirical techniques. After the polymer has solidified or has been cured sufficiently, the coated stent and the core pin are removed from the mold as a unit and then the core pin and pin cap are removed from the stent. Successive molding operations with differently sized core pins or outer molds allow layers of different materials to be built up on either the internal or exterior surface of the stent.

[0020] An alternative embodiment obviates the use of the core pin and cap described above, whereby a preformed polymer sheath is inserted into the stent initially. By subsequently applying polymer in its liquid state to the exterior of the stent, the sheath becomes joined to the applied polymer and, thus, the stent becomes completely encased in polymer. The pre-formed nature of the sheath serves to precisely define the thickness of polymer that will be applied to the interior surface of the stent. A dip coating process without use of an exterior mold allows the polymer to be built up selectively on the exterior side of the stent, while the use of an external mold positively limits its external thickness. The polymer from which the sheath is pre-formed does not have to correspond, necessarily, to the polymer that subsequently is applied in its flowable form, thus disparate types of polymer can be applied to the surfaces of the stent.

[0021] FIG. 3 illustrates the preferred method of practicing this embodiment. The polymer sheath 24 that is to comprise the inner surface of the finished product first is applied to a teflon or silicon support tube 22, either by dip coating or extrusion. The metal stent 12 then is slipped over the coated tube, and then a tapered mandrel 26 is inserted into the tube. The taper 28 of the tapered mandrel facilitates insertion and expands the polymer sheath snugly against the interior surface of the stent 12. The exterior of the stent then is coated with polymer, either by dipping or pull trusion without an exterior mold, or by injection molding with the use of an external mold. After curing, the tapered mandrel 26 and the support tube 22 are removed to provide a fully coated stent.

[0022] Depending upon the type of stent structure to which the polymer is applied, it may be necessary to remove some of the polymer or at least to cut the polymer at selected sites in order to restore the requisite flexibility to the stent. In a multi-link stent, for example, the various links must be able to undergo relative movement during the expansion of the device. The presence of polymer or at least the presence of a continuous mass of polymer between the links could inhibit relative movement and thus inhibit expansion of the stent during deployment. In order to prevent such inhibition of movement or expansion, it is necessary either to remove or, at the very least, to perforate the polymer in such locations. The preferred method of doing so is with the use of a laser, with which device polymer material can be quickly and precisely penetrated as required.

[0023] With certain stent configurations, it is advantageous to apply polymer to the stent while the stent is in the expanded state. The stent initially is expanded, such as by advancing the core pin and the pin cap towards one another to force the stent sufficiently high up along the tapered surface to achieve its deployed diameter. Alternatively, an oversized sheath and mandrel may be used. Any of the various alternative embodiments described above then may be utilized to apply the polymer. For certain stent configurations, application of the polymer while the stent is in the expanded state results in less "webbing" between the struts and yields greater mechanical stability in the final product. Additionally, the final polymer coating may need little or no laser processing for separation or clean up before the stent is contracted down to its pre-delivery outer diameter or "O.D."

[0024] After the stent is coated and trimmed, a therapeutic agent or agents can be loaded at desired concentration levels, in accordance with methods that are well-known in the art, to render the device ready for implantation.

[0025] While a particular form of the invention has been illustrated and described, it also will be apparent

to those skilled in the art that various modifications can be made without departing from the scope of the invention. Accordingly it is not intended that the invention be limited except by the appended claims.

Claims

1. A method for coating a stent, comprising the steps of:

   providing a stent (12) having a generally cylindrical shape, the stent having an interior surface and an exterior surface;
   securely positioning a mandrel (14 and 15, 26) within the stent to define a space of substantially constant thickness (19) between the mandrel and said interior surface of the stent;
   contacting the mandrel-containing-stent with a polymer in a flowable state;
   allowing the polymer to transform to a substantially non-flowable state; and
   removing the mandrel from the stent.

2. The method of claim 1, wherein the mandrel-containing-stent is contacted with the polymer so as to coat the exterior surface of the stent (12) with a layer of polymer having a thickness that is greater than the thickness of the space (19) between the mandrel (14 and 15, 26) and the interior surface of the stent.

3. The method of claim 1 wherein the stent (12) is contacted with the polymer by submerging the stent in a mass of the polymer while the polymer is in a flowable state.

4. The method of claim 1 wherein the stent (12) is contacted with the polymer by a pull trusion technique.

5. The method of claim 1 further comprising the step of re-contacting the mandrel-containing-stent with the polymer in while the polymer is in a flowable state after the polymer with which the stent previously had been contacted has transformed a substantially non-flowable state and prior to the removal of the mandrel (14 and 15, 26) whereby the exterior and interior surfaces of the stent become differentiated in terms of the thickness of the polymer coatings thereon.

6. The method of claim 1, further comprising the step of contacting the stent (12) with a second polymer while the second polymer is in a flowable state after said first polymer has become transformed to a substantially non-flowable state and prior to the removal of the mandrel (14 and 15, 26) whereby the exterior and interior surfaces of the stent become differentiated in terms of the types of the polymers coated thereon.

7. The method of claim 1 wherein the mandrel comprises a core pin (14) and a pin cap (16), wherein the pin cap slidably receives the distal end of the core pin and wherein both the core pin and the pin cap include a conical surface that extends to diameter greater than that of the stent, the method further comprising the step of advancing the pin cap along the core pin, whereby the stent (12) becomes coaxially secured in position relative to the core pin.

8. A method for coating a stent, comprising the steps of:

   providing a stent (12) having a generally cylindrical shape, the stent having an interior surface and an exterior surface;
   securely positioning a mandrel (14 and 15, 26) within the stent to define a first space (19) of a substantially constant first thickness between the mandrel and the interior surface of the stent;
   securely positioning the mandrel-containing-stent within an exterior mold (20) to define a second space of a substantially constant second thickness between the exterior mold and the exterior surface of the stent;
   introducing a polymer in a flowable state into the first and second spaces;
   allowing the polymer to transform to a substantially non-flowable state; and
   removing the exterior mold from about the stent and the mandrel from within the stent.

9. The method of claim 8, wherein the first thickness is greater than the second thickness.

10. The method of claim 9 wherein the second thickness is greater than the first thickness.

11. The method of claim 8, further comprising the steps of:

   removing only the exterior mold (20) from about the stent after the polymer has transformed into a substantially non-flowable state;
   securely positioning the mandrel-containing-stent within a second exterior mold to define a third space between the exterior surface of the first polymer coated stent and the second exterior mold; and
   introducing a second polymer in a flowable state into the third space.

12. A method of coating a stent, comprising the steps of:

providing a stent (12) having a generally cylindrical shape, the sent having an interior surface and an exterior surface ;
fitting a sheath (24) pre-formed of a first polymer within the stent;
contacting the stent with a second polymer in a flowable state; and
allowing the second polymer to transform into a substantially non-flowable state.

13. The method of claim 12 wherein the first and second polymers are the same.

14. The method of claim 12 wherein the first and second polymers are different.

15. The method of claim 12, further comprising the step of inserting a mandrel (14 and 15, 26) into the sheath (24) of the first polymer fitted within the stent (12) in order to expand the sheath of the first polymer against the interior surface of the stent.

16. The method of claim 15, wherein the mandrel has a tapered tip.

17. The method of claim 12, further comprising the step of securely positioning the sheath-containing-stent within an exterior mold to define a space between the exterior surface of the stent, the mold having a constant first thickness.

18. The method of claim 17, wherein the sheath (24) of the first polymer has a constant second thickness and wherein the first and second thickness are equal.

19. The method of claim 17, wherein the cylinder of polymer has a constant second thickness and wherein the first and second thickness are not equal.

20. The method of claim 19 wherein the first thickness is greater than the second thickness.

21. The method of claim 19 wherein the second thickness is greater than the first thickness.

FIG. 1

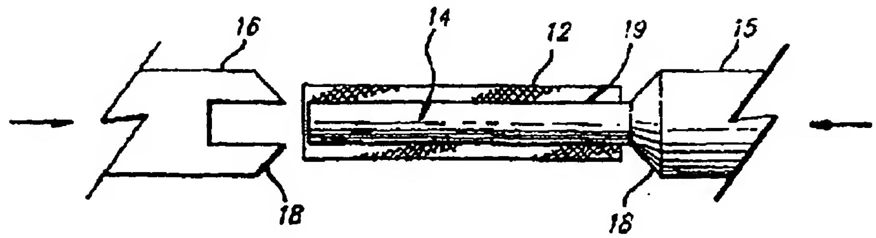


FIG. 2

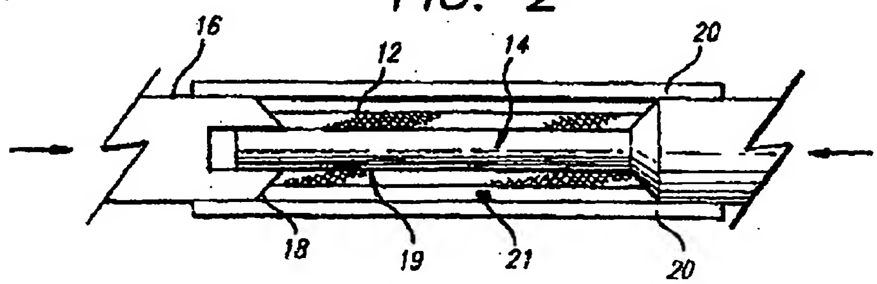
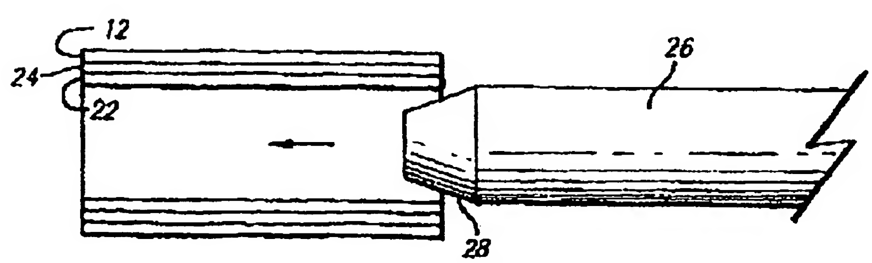


FIG. 3



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